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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/424,059	11/18/99	NUNOKAWA	Y	001560-376

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1624	8

DATE MAILED: 01/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/424,059	Applicant(s) NUNOKAWA ET AL.	
	Examiner Tamthom N. Truong	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

NON-FINAL ACTION

Applicant's amendment filed on 11-2-00 has overcome the previous rejection under 35 U.S.C. 112, second paragraph. Thus, said rejection is withdrawn herein. However, the amended claims have not overcome the previous rejections under 35 U.S.C. 112, first paragraph, and 103. The amended and new claims also incur issues of 112, second paragraph, and 102 (a)/(b).

Note, the amendment to claim 14 cannot be entered as the term "inhibitor" is not in said claim.

Pending claims 1-41 are considered herein.

Specification

Improper Incorporation By References: The preparation of compounds of formula I is an essential material which can only be incorporated by references to US patents, and not to foreign documents such as JP (kokai) 62-286949, and the article from Chem. Pharm. Bull. (as cited on page 24). Applicant is reminded that the incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See ***In re Hawkins***, 486 F.2d 569, 179 USPQ 157 (CCPA 1973).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-41are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claims 1, 14, 16, 29, 30, and 38-41 recite the limitation, "carboxyl group which is **optionally** esterified or amidated", which is unclear as to the structural make-up of ester, and amide groups.

b. Claims 1, 5, 9, 14, 16, 19, 20, 24, 29, 30, and 38-41 recite several phenyl groups for variable Z. However, said groups are not separated by commas. Thus, it is unclear whether said groups are meant as alternatives, or are meant to be linked to each other.

c. Claims 10-13 are substantial duplicates because they all recite the same composition with different intended uses in the preambles. Preambles do not have patentable weight unless they "breath life into the claims".

d. Claim 20 is an improper multiple dependent claim because it does not refer to previous claims in the alternative language.

e. Claims 14, 29 and 30 are substantial duplicates because they all recite the same compounds for different intended uses. Said uses are considered as preambles which do not have patentable weight.

f. Claims 25-28 are substantial duplicates because they all recite the same composition with different intended uses. Said uses are considered as preambles which do not have patentable weight.

g. Claims 38 and 39 are substantial duplicates because they recite the same method even though the wording is different. Ultimately, a disease caused by the activation of NF-κB must be treated by NF-κB inhibition.

h. Claims 40 and 41 are substantial duplicates because they recite the same method even though the wording is different. Ultimately, a disease caused by the excessive production of TNF-α must be treated by TNF-α inhibition.

i. Claims 1, 14, 16, 29-41 recite the phrase "benzoquinone derivative" is unclear as to the nature and the site where formula I can be derived into another compounds.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 29, and 38-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of diseases related to NF-κB, and TNF-α using compounds of formula I, does not reasonably provide enablement for the **prevention** of said diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. While the disclosure shows the inhibitory activity of NF-κB and TNF-α for a subset of compounds of formula I, said evidence does not provide sufficient guidance for one skilled in the art to prevent diseases associated with NF-κB, and TNF-α. For a "preventive therapy", one would have to know the time frame for administration, the dosage and the prognosis. For examples, diseases such as osteoarthritis, rheumatoid arthritis, Alzheimer's, multiple organ failure, etc. do not occur in everyone, and do not have a 'chemical marker' that one can predict the onset of such diseases. So, it is impossible to develop a "preventive therapy" without undue experimentation.

Additionally, claims 1-14, and 16-41 are rejected herein for relying on the improper incorporation by references for essential material as discussed in the objection to the disclosure above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-14, 16-34, and 37 are rejected under 35 U.S.C. 102 (a)/(b) as being anticipated by **Suzuki et. al.** (Chem. Pharm. Bull., vol. 45 (4), pp. 668-674): On page 668, Suzuki et. al. reveal compound #1 which is embraced by the compound claims 14, 29-34, and 37. Note, R_1 in the reference corresponds to R_1 and R_2 herein. Also, R_3 in the reference corresponds to $(CH_2)_n$-R_4, wherein R_4 represents $-COOR_5$. Furthermore, the intended uses recited in said claims have no patentable weight since they do not result in structural changes of the compounds.

Composition claims 1-13, and 16-28 are essentially pharmaceutical compositions, and inherently embraced in the above reference because the taught compounds possess pharmaceutical properties.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-34, and 37 are rejected under 35 U.S.C. 102 (a)/(b) as being anticipated by the following references:

Tatsuoka (JP-62-286949): On page 318, Tatsuoka discloses compound (1b) that is embraced by compound claims 14, 29-34 when the claimed formula I has substituents such as: hydrogen for R_1–R_3; one of the phenyl groups for Z; 0 for n, and –$COOR_5$ for R_4.

Suzuki et. al. (Chem. Pharm. Bull., Vol. 44 (1), pp. 139-144): On page 140, Suzuki et. al. disclose compounds 2c, 2d, and 2e which are embraced by compound claims 14, 15 (species on line 17, page 116), 29-34, and 37. Like the above references, different intended uses do not have patentable weight, and thus, anticipation prevails.

Composition claims 1-13, and 16-28 are essentially pharmaceutical compositions, and inherently embraced in the above references because the taught compounds possess pharmacological properties (e.g., brain-protective action, and platelet aggregation inhibition), and thus, pharmaceutical composition is understood. Although the composition claim recite different intended uses in their preambles, said preambles do not have patentable weight because they do not result in structural changes in said compositions.

Thus, at the time of the invention, one skilled in the art would have known how to make the claimed compounds and compositions in view of the teaching of Tatsuoka, and Suzuki et.al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following analysis is based on factual inquiries set forth in ***Grahm et. al. v. John Deere Co.*** (148 USPQ 459), and pertinent case laws in chemical art.

Claims 1-34, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Tatsuoka** (JP'949), and **Suzuki et. al.** As discussed in the 102 rejections above, compounds of said references, wherein R_4 is at the *meta* position of the phenyl ring represented by Z, are embraced by the claimed formula I. However, said compounds are also positional isomers of other compounds of the claimed formula I, wherein R_4 is at the *ortho-* or *para-* position of said phenyl ring. Note, Tatsuoka teaches side chain attachment at all ring positions corresponding to the instant. Positional isomers are expected to have the share the same physiological activity, and thus, are not deemed patentably distinct absent evidence of superior unexpected results as

has been ruled in **In re Crounse**, 150 USPQ 554; **Ex parte Engelhardt**, 208 USPQ 343 regarding positional isomerism.

Furthermore, on page 315, Tatsuoka reveals a genus of formula (1) which reads on other species of the claimed formula (I) in compound claims 14-37. Note, the claimed formula I and the disclosed formula I have the same variables which cover the same set of substituents. Even though the intended uses are different for both genera, said uses are recited as preambles which have no patentable weight as they do not result in structural changes. Thus, with respect to genus-species situations, the M.P.E.P. states that "a generic chemical formula will anticipate a claimed species covered by the formula when the species can be "at once envisaged" from the formula." (M.P.E.P. 2131.02) Such an issue of patentability has also been decided by the court in **In re Susi**, 440 F 2d. 442, 445, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in **Merck & Co. v. Biocraft Laboratories**, 874 F 2d. 804, 10 USPQ 2d. 1843, 1846 (Fed. Cir. 1989), and **In re Swinehart**, 169 USPQ 225, 229 (CCPA 1971).

Even though, said references teach different utility, one of the ordinary skill in the art still would have been motivated to select compounds of the claimed formula I. The reason for that is because one would have expected said compounds to have the same utility as those disclosed by Tatsuoka and Suzuki et. al. See **In re Dillon** 16 USPQ 2d. 1897, 1923 regarding a prima facie case of obviousness of structurally similar compounds disclosed by a prior art "regardless of the properties disclosed in the inventor's application".

Thus, at the time of the invention, it would have been obvious for one skilled in the art to make compounds of the claimed formula I, wherein R_4 is at the *ortho-* and *para-* positions of the phenyl ring represented by Z, in view of Tatsuoka and Suzuki et. al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom (or Tam) N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

The fax phone number for the organization where this application or proceeding is assigned is 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong / 1-2-00

JOHN M. FORD
PRIMARY EXAMINER
GROUP 1620 - ART UNIT 1624

SUPERVISORY PATENT EXAMINER
ART UNIT 1624